

**REMARKS**

Claims 1-6, 11-25 and 46-49 are pending. No new matter has been added by way of the present amendments. For instance, the specification and Abstract of the Disclosure have been amended to correct minor typographical and grammatical errors. Claim 1 has been amended to more clearly define the present invention and the Examiner is referred to the present specification at page 9, lines 18-20, page 15, lines 19-21, page 25, lines 6-10 and the Figures.

Claims 3 and 5 have been amended to refer to the first and second heterologous conjugates, respectively. Claim 6 has been amended to recite that the first and second proteins of interest specifically bind to one another as supported by the present specification at page 8, lines 24-27. New claim 47 is supported by the present specification at page 6, lines 6-24. New claim 48 is supported by the present specification at page 10, lines 5-6. Lastly, new claim 49 is supported by the present specification at page 11, lines 7-10. Accordingly, no new matter has been added.

In view of the following remarks, Applicant respectfully requests that the Examiner withdraw all rejections and allow the currently pending claims.

***Election/Restriction***

In the outstanding Office Action, the Examiner indicates that

claims 1-6 of Group I will be rejoined in part with the claims of Group II. The Examiner has therefore searched and considered the claims of Group I as well as claims 11-25 of Group II (the Examiner has maintained that claims 8-10 will be withdrawn).

Applicant thanks the Examiner for considering claims 11-25. However, Applicant wishes to point out two issues. First, although the Examiner indicates that claims 11-25 of Group II will be rejoined and examined, claim 12 has been withdrawn from consideration. Applicant believes that this may be due to the fact that claim 12 is drawn to a non-elected species, however, due to the improper nature of the Examiner's prior art rejection, as explained below, claim 12 should be rejoined with the remainder of the claims. Second, claim 7, belonging to a non-elected invention has been included in the Examiner's rejections. Applicant submits that claim 7 belongs to Group III, and should be not be under consideration, and therefore has been cancelled.

Applicant has limited the present claims to those claims which should be properly examined in the present application. Applicant hereby reserves the right to file divisional applications directed to the non-elected invention.

#### ***Objections to the Specifications***

The Examiner has objected to the specification for the reasons outlined on page 3 of the Office Action. Applicant traverses.

First, the Examiner asserts that the specification refers to a drawing, Figure 1E, however, there is no Figure 1E. Applicant disagrees with the Examiner and submit that the label of Figure 1E appears to have been obscured by the photocopy submitted to the PTO. This issue will be corrected once formal drawings are submitted.

Second, the Examiner asserts that several spelling errors exist in the specification. Applicant traverses and submits that the present amendment rectifies this error.

Accordingly, each of the Examiner's objections are moot. Reconsideration and withdrawal thereof are respectfully requested.

***Information Disclosure Statement***

The Examiner states that the listing of references in the specification is not a proper Information Disclosure Statement. Applicant agrees and submit that the listing of references on pages 29-31 is simply a list of supporting documents.

***Issues Under 35 U.S.C. § 112, First Paragraph***

The Examiner has rejected claims 1-7, 11, 13-22, 24, 25 and 46 under 35 U.S.C. § 112, first paragraph, for the reasons recited at pages 4-8 of the outstanding Office Action. Applicant respectfully traverses this rejection.

The Examiner asserts that the specification is enabling only for GFP as the detectable group and iosforms of CaMKII  $\alpha$  and  $\beta$ .

Applicant respectfully disagrees with the Examiner.

As explained at the Interview conducted on March 25, 2003, the present invention relates to a two hybrid system for detecting protein-protein interactions. The simplicity of the system (two heterologous conjugates) and the advanced information gained (detailed knowledge of interacting proteins not only in the cellular environment but in a specific location within the cell, as chosen with the anchor protein) point to the full utilization of the cellular machinery. If two proteins of interest do not interact, the detectable group will be localized anywhere in the cell primarily dictated by the behaviour of the first protein of interest. However, when the two proteins of interest interact, the location of the detectable group will mimic the location of the internal structure. Only in the case of the two proteins interacting, will this localization occur. The prior knowledge of location of the internal structure can be obtained e.g. from Shirai, disclosing the membrane localization of PKC. In other words, the assay system described in the amended claims contains a built-in control.

Accordingly, the internal structure and protein which specifically binds to the internal structure may vary. Concerning the first and second proteins interest, Applicant respectfully submits that it is exactly these proteins which may be unknown. Rather, it is the mechanism currently claimed which is to be used in the determination of binding interactions between the first and

second proteins of interest. Accordingly, Applicant respectfully submit that the present claims are fully enabled by the present specification.

***Issues Under 35 U.S.C. § 112, Second Paragraph***

The Examiner has rejected claims 1-7, 11, 13-25 and 46 under 35 U.S.C. § 112, second paragraph, for the reasons recited at pages 8 and 9 of the outstanding Office Action. Applicant respectfully traverses these rejections.

First, the Examiner has rejected claim 1 asserting that it is incomplete for missing an essential step. Applicant respectfully disagrees and submits that claim 1 has been amended to more clearly define the required steps. Thus, this rejection is moot.

Additionally, the relationship between the structures required in claim 1 have been clarified.

Second, the Examiner asserts that claims 3 and 4 are indefinite for the recitation of a "nucleic acid" that encodes a fusion protein. The Examiner asserts that this broadens the base claim. Applicant traverses and submits that the claims have been clarified in this regard.

Third, the Examiner has rejected claim 6 asserting that "members of a specific binding pair" is ambiguous. Applicant traverses and submits that this is a phrase well known in the art. However, in an effort to expedite prosecution, Applicant has amended claim 6 to remove this language.

Fourth, the Examiner has rejected claim 7 asserting that it broadens claim 1. Applicant traverses and submits that claim 7 was non-elected and has been cancelled.

Fifth and lastly, the Examiner has rejected claims 24 and 25 asserting that it is unclear what aspects of the two proteins are the "same" or "different". Applicant traverses and directs the Examiner's attention to the present specification at page 1, lines 13-15. Based upon this disclosure, it is evident that term "same" refers to the situation where the two proteins form a timer or oligomer. The language "different" refers to situations where the two proteins are, in fact, distinct proteins.

In view of the above, Applicant respectfully submits that the present claims fully satisfy the requirements of 35 U.S.C. § 112, second paragraph. Reconsideration and withdrawal of these rejections is therefore requested.

***Issues Under 35 U.S.C. § 102(a)***

The Examiner has rejected claims 1-6, 11, 15-22, 24, 25 and 46 as being anticipated by Shirai. Applicant respectfully traverse this rejection.

Shirai relates to a fusion of PKC and GFP. This is a disclosure of only a single conjugate. Shirai fails to suggest or disclose the two heterologous conjugates of the present invention. Accordingly, no anticipation exists based upon Shirai.

The Examiner has also rejected claims 1-7, 11-14, 15-22, 24,

25 and 46 as being anticipated by Knippschild. Applicant traverses.

Similar to the distinction with respect to Shirai, Knippschild discloses only a single fusion protein of gamma and epsilon kinase with GFP. Knippschild fails to suggest or disclose utilizing a second protein of interest fused to a known protein. Accordingly, no anticipation exists based upon Knippschild. Reconsideration and withdrawal of this rejection are respectfully requested.

In view of the above, Applicant respectfully submits that the present claims define subject matter which fully satisfies the requirements of 35 U.S.C. § 112, first paragraph, and which is distinct from the cited art. Accordingly, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

If the Examiner has any questions or comments, please contact Craig M. McRobbie, Reg. No. 42,874 at the offices of Birch, Stewart, Kolasch & Birch, LLP at (703) 205-8000 in the Washington, D.C. area.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of two (2) months to April 20, 2003 in which to file a reply to the Office Action. The required fee of \$205.00 is enclosed herewith.


If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

Application No.: 09/787,792

overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made